IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

TEVA PHARMACEUTICALS USA, INC.	:	CIVIL ACTION
v.	:	
AMGEN, INC.	:	NO. 09-5675

MEMORANDUM

Dalzell, J. September 10, 2010

Plaintiffs/Counter-defendants Teva Pharmaceuticals USA, Inc., and Teva Pharmaceuticals Ltd. ("Teva") seek a declaratory judgment against Amgen, Inc. that two of Amgen's patents are invalid. Defendants/counter-claimants Amgen Inc. and Amgen Manufacturing, Limited ("Amgen") have countersued Teva seeking a declaratory judgment to the effect that, once Teva starts to sell its product in the United States, it will infringe on Amgen's two patents-in-suit.

I. The Patents-In-Suit

The patents at issue in this case are United States Patent No. 5,580,755, entitled "Human Pluripotent Granulocyte Colony-Stimulating Factor" ("the '755 patent"), and United States Patent No. 5,582,823, entitled "Methods of Treating Bacterial Inflammation and Granulocytopoiesis By Administering Human Pluripotent Granulocyte Colony-Stimulating Factor" ("the '823 patent")(collectively, the "Amgen patents" or the "patents-in-suit"). Amgen owns these patents and used them to develop

Filgrastim. Amgen asserts that Filgrastim falls within the scope of claim 1 of the '755 patent. Amgen markets its Filgrastim product in America as a parenteral solution under the trademark Neupogen®. Neupogen® is administered to patients to treat neutropenia (an abnormal or dramatic decrease in the number of a kind of white blood cells, neutrophils, which help the body fight infection) by stimulating white blood cell production, thereby reducing the risk of infection to patients undergoing treatments such as chemotherapy. Amgen has also developed a product called Neulasta® which is based upon Filgrastim. The active ingredient in Neulasta® is Pegfilgrastim, a covalent conjugate of Filgrastim and monomethoxypolyethylene glycol. Amgen claims that Pegfilgrastim and its use fall within the scope of one or more claims of the '755 and '823 patents. The '755 Patent will expire on December 3, 2013. The '823 Patent will expire on December 10, 2013.

Teva has developed a Filgrastim-containing product called Neutroval, which has already been approved for sale in Europe. Teva began selling the product in Europe (where Amgen's patents expired in 2006) in November of 2008. Teva believes that it will receive FDA approval for Neutroval before Amgen's patents expire. Teva intends to sell it in the United States in advance of the expiration of Amgen's patents and without a license from

Amgen.

Teva seeks a declaratory judgment that the '755 and '823 patents are invalid. Amgen seeks a declaratory judgment that Teva is infringing on its patent, and seeks to enjoin Teva from selling Neutroval in the United States. Amgen also requests an accounting of all products Teva has made that contain Filgrastim that Teva has imported, sold, used or offered to sell in the United States. To the extent that Teva imported, sold, used or offered to sell the products in this country, Amgen seeks damages for lost profits.

II. Background

Dr. Lawrence M. Souza invented the patents-in-suit that Amgen owns. Before Dr. Souza's inventions, no one had successfully obtained or made an isolated human pluripotent granulocyte colony-stimulating factor polypeptide ("hpG-CSF") product that could effectively treat neutropenia. In 1985, Dr. Souza succeeded in isolating and sequencing DNA that encodes a species of human G-CSF. Using Dr. Souza's inventions, Amgen developed Neupogen®.

Teva has developed a product to compete with Neupogen® and filed a Biologics License Application ("BLA") with the U.S. Food & Drug Administration on November 30, 2009. If the FDA approves Teva's BLA, Teva's product will be the first competing

filgrastim drug product in this country. Teva's Opening Brief on Claim Construction ("Teva Br.") at 7.

Now before us are the parties' requests for claim construction pursuant to Markman v. Westview Instrument, Inc., 52 F.3d 967 (Fed. Cir. 1995)(en banc), aff'd, 517 U.S. 370 (1996). On August 13, 2010, we heard protracted oral argument on claim construction. The following discussion explains our reasoning as to each contested claim construction.

III. Standards for Claim Construction

Courts give claim terms their ordinary and accustomed meaning as understood by one of ordinary skill in the pertinent art at the time of filing. Phillips v. AWH Corp., 415 F.3d 1303, 1312-13 (Fed. Cir. 2005)(en banc). "It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." Id. at 1312 (internal quotation marks omitted). Construing the claims of a patent presents a question of law. See Markman, 52 F.3d at 977-78. "[T]here is no magic formula or catechism for conducting claim construction." Phillips, 415 F.3d at 1324. Instead, the court is free to attach the appropriate weight to relevant sources "in light of the statutes and policies that inform patent law." Id.

The words of a claim are generally given their ordinary

and customary meaning, which is "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." Id. at 1313 (internal citations and quotation marks omitted). "[T]he ordinary meaning of a claim term is its meaning to the ordinary artisan after reading the entire patent." Id. at 1321 (internal quotation marks omitted). The patent specification "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d, 1576, 1582 (Fed. Cir. 1996).

While "the claims themselves provide substantial guidance as to the meaning of particular claim terms," a court must also consider the context of the surrounding words of the claim. Phillips, 415 F.3d at 1314. And because claim terms are normally used consistently throughout the patent, "[o]ther claims of the patent in question, both asserted and unasserted, can also be valuable sources of enlightenment." Id. (internal citation omitted).

Differences among claims can also be a useful guide. For example, "the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the

limitation in question is not present in the independent claim." Id. at 1314-15 (internal citation omitted). This "presumption is especially strong when the limitation in dispute is the only meaningful difference between an independent and dependent claim, and one party is urging that the limitation in the dependent claim should be read into the independent claim." SunRace Roots Enter. Co., v. SRAM Corp., 336 F.3d 1298, 1303 (Fed. Cir. 2003).

The language in the specification "may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." Phillips, 415 F.3d at 1316. And "[e]ven when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction," Liebel-Flarsheim Co. v. Medrad, Inc., 358 F.3d 898, 906 (Fed. Cir. 2004) (internal quotation marks omitted), aff'd, 481 F.3d 1371 (Fed. Cir. 2007) (after earlier remand).

In addition to the specification, a court "should also consider the patent's prosecution history, if it is in evidence." Markman, 52 F.3d at 980. The prosecution history, which is "intrinsic evidence, consists of the complete record of the

proceedings before the [Patent and Trademark Office ("PTO")] and includes the prior art cited during the examination of the patent." Phillips, 415 F.3d at 1317 (internal quotation marks omitted). "[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." Id.

A court may also rely upon "extrinsic evidence," which "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." Markman, 52 F.3d at 980. For instance, technical dictionaries can assist the court in determining the meaning of a term to those of skill in the relevant art because such dictionaries "endeavor to collect the accepted meanings of terms used in various fields of science and technology." Phillips, 415 F.3d at 1318. In addition, expert testimony can be useful "to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field."[1] Id. Nonetheless, courts must not lose sight of the

[1]The parties did not proffer any expert testimony.

fact that "expert reports and testimony [are] generated at the time of and for the purpose of litigation and thus can suffer from bias that is not present in intrinsic evidence." Id. Overall, while extrinsic evidence "may be useful" to the court, it is "less reliable" than intrinsic evidence, and its consideration "is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." Id. at 1319.

Finally, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." Renishaw PLC v. Marposs Societa' per Azioni, 158 F.3d 1243, 1250 (Fed. Cir. 1998). It follows that "a claim interpretation that would exclude the inventor's device is rarely the correct interpretation." Modine Mfg. Co. v. United States Int'l Trade Comm'n, 75 F.3d 1545, 1550 (Fed. Cir. 1996), abrogated on other grounds by Festo Corp. V. Shoketsu Kinzoku Kogyo Kabushiki Co., 234 F.3d 558 (Fed. Cir. 2000), quoted in Osram GmbH v. Int'l Trade Comm'n, 505 F.3d 1351, 1358 (Fed. Cir. 2007). Thus, if possible, claims should be construed to uphold validity. See In re Yamamoto, 740 F.2d 1569, 1571 (Fed. Cir. 1984).

IV. Construction of the Disputed Terms

The parties present five disputed claim terms or phrases from the two patents-in-suit. The first claim of the '755 patent has disputed terms as does the second claim of the '823 patent. Claim 1 of the '755 patent states, "[a]n isolated human pluripotent granulocyte colony stimulating factor (hpG-CSF) polypeptide having an amino acid sequence selected from the group consisting of: [+1 Thr to +174 Pro]; and [-1 Met to +174 Pro]; and analogs thereof wherein one or more of the cysteines residues located at positions 17, 36, 42, 64, and 74 are replaced by serine." Claim 2 of the '823 patent states, "[a] method for providing granulocytopoietic therapy to a mammal comprising administering an effective amount of a hpG-CSF polypeptide having an amino acid sequence selected from the group consisting of: [+1 Thr to +174 Pro]; and [-1 Met to +174 Pro]; and analogs thereof wherein one or more cysteines residues located at positions 17, 36, 42, 64, and 74 are replaced by serine."

A. "Pluripotent" and "p" (signifying "pluripotent") (Claim 1 of the '755 patent and Claim 2 of the '823 patent)

Claim Term	Amgen's Construction	Teva's Construction
"Human Pluripotent Granulocyte Colony Stimulating	A species of human polypeptide, designated "hpG-CSF"	"pluripotent", which should be pulled out from the term and has its own meaning -- capable of generating

Factor" or "hpG-CSF"		numerous cell types -- is ignored by Amgen's construction

Amgen argues that the term "human pluripotent granulocyte colony stimulating factor" or "hpG-CSF" is a term the inventor, Dr. Souza, coined, which meant to refer to the newly-identified polypeptides encoded by DNA sequences that he first cloned and characterized from human cells and which was never meant to be parsed into its individual component words. Amgen asserts that the specification confirms that "an hpG-CSF" is merely a name for a sequence-defined polypeptide, and that the name simply refers to the encoded human polypeptide that has the defining 1-174 sequence of amino acids. Amgen's Corrected Claim Construction Brief ("Amgen Br.") at 23; Amgen Resp. at 5.

Amgen contends that Teva improperly uses a dictionary and not the specification to impart limitations not required by the claim language or supported in the specification or prosecution history. Amgen argues that the term is used in the specification merely to designate the claimed polypeptide as hpG-CSF. Amgen Resp. at 5. Dr. Souza, in order to differentiate his polypeptides from others' previous preparations,[2] "coined a hybrid term" as a naming convention,

[2]The others are Karl Welte and Nicos Nicola, who each contributed to the prior art.

drawing a conceptual connection between the prior preparations and his claimed species of polypeptide. Id. at 6. Amgen claims that hpG-CSF is just the polypeptide's name, and does not actually indicate that the polypeptide is pluripotent. Amgen points out that hpG-CSF is used in the specification to refer to polypeptides that are variations of the common 174-amino acid core sequence, and, thus, could have one or more of the biological properties of naturally occurring hpG-CSF. Amgen Br. at 24.

Amgen also argues that pluripotent polypeptides can "enhance" granulocyte production but cannot "generate" cells in the sense that pluripotent cells can. According to Amgen, pluripotent polypeptides are a different animal and do not "generate" cells. Amgen Resp. at 10-11.

Teva argues that "pluripotent" means "capable of generating numerous cell types," and that Amgen has improperly removed "pluripotent" from the claims. Teva Br. at 17. Teva also contends that Amgen's construction means that the polypeptide does not have to be actually pluripotent, but must only be designated pluripotent. Teva claims this is improper because all of the words of a claim are presumed to limit the claim and give it meaning. Id. at 18. Teva argues that the plain and ordinary meaning of pluripotent is "having the ability

to generate numerous cell types." Id. at 19. This means that hpG-CSF causes human bone marrow cells to proliferate and differentiate. Markman Hr'g Tr. at 77, Aug. 13, 2010.

We must give meaning to all of the words in Amgen's claims. Exxon Chemical Patents, Inc. v. Lubrizol Corp., 64 F.3d 1553, 1557 (Fed. Cir. 1995). "Pluripotent" implies biological activity, of which Amgen now disputes the limiting necessity. But the specification suggests that the product is pluripotent in fact -- not just designated pluripotent: "[t]he present application pertains in particular to mammalian pluripotent colony stimulating factors...." '755 Patent at 1:18-20 (emphasis added); "Novel DNA sequences of the invention include sequences useful in securing expression in procaryotic or eucaryotic host cells of polypeptide products having at least a part of the primary structural conformation and one or more of the biological properties of naturally occurring pluripotent granulocyte colony-stimulating factors." Id. at 3:38-43 (emphasis added).

The specification states that the claimed polypeptide has one or more of the biological properties of naturally existing hpG-CSF, id. at 2:53-55; 2:59-65, and also describes the pluripotent functionality of the product, id., at 20:12-50. The specification explains that "[i]t is noteworthy that activity is not necessary for any one or more of the products of the

invention to have therapeutic utility." Id., 24:66-25:3 (emphasis added). Amgen claims that during prosecution Dr. Souza "made clear" that his claimed hpG-CSF polypeptide was distinguished by its amino acid sequence (and not, presumably, by its biological activity). Amgen Br. at 24. This does not indicate, however, regardless of necessity, whether the polypeptide will be pluripotent. The name and the details of the specification seem to suggest that it will be actually pluripotent, or, at least, that was the understanding at the time of the patent's filing.

Amgen claimed during oral argument that the Federal Circuit has held that although every term in a claim must have meaning, this does not mean that every word must have a meaning. Markman Hr'g Tr. at 86, Aug. 13, 2010. This is not correct. The Federal Circuit has held that "[w]e must give meaning to all the words in [the patent holder's] claims." Exxon Chemical Patents, 64 F.3d at 1557 (emphasis added)(citing In re Sabatino, 480 F.2d 911, 913, 178 USPQ 357, 358 (CCPA 1973)). The specification indicates that the product in question will be pluripotent. All of the terms of a claim are presumed to limit the claim and give it meaning. Bicon, Inc. v. Straumann Co., 441 F.3d 945, 950 (Fed. Cir. 2006)("Allowing a patentee to argue that physical structures and characteristics specifically described in a claim

are merely superfluous would render the scope of the patent ambiguous, leaving examiners and the public to guess about which claim language the drafter deems necessary to his claimed invention and which language is merely superfluous, nonlimiting elaboration. For that reason, claims are interpreted with an eye toward giving effect to all terms in the claim."). Because Dr. Souza understood the product to be "pluripotent" at the time the patent was filed, it is improper for Amgen to try to remove the requirement that the polypeptide be pluripotent. In addition, during prosecution, Amgen included the following amendment: "Please note that the title of the invention has been changed to make it more specific to the claimed invention: "HUMAN PLURIPOTENT GRANULOCYTE COLONY-STIMULATING FACTOR," suggesting that the name reflects the characteristics of the product. Amgen Claim Constr. Br., Ex. 18 at AMT 00002464 ('755 Prosecution History, 12/4/95 Notice of Allowability, Paper No. 31).

Amgen included "pluripotent" as a limitation in its claim, and we cannot now read that limitation out of it. Exxon Chemical Patents, 64 F.3d at 1557. Thus, Amgen "must live with the language it chose." Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp., 93 F.3d 1572, 1583 (Fed. Cir. 1996). We will adopt Teva's construction of this term.

B. "Having An Amino Acid Sequence Selected From the Group Consisting Of..." (Claim 1 of the '755 patent and Claim 2 of the '823 patent)

Claim Term	Amgen's Construction	Teva's Construction
"having an amino acid sequence selected from the group consisting of"	having an amino acid sequence selected from the following three amino acid sequences	having one and only one of the following three amino acid sequences, including impurities

The language in the claims -- "an amino acid sequence selected from the group consisting of: [+1 Thr to +174 Pro]; and [-1 Met to +174 Pro]; and analogs thereof wherein one or more cysteines residues located at positions 17, 36, 42, 64, and 74 are replaced by serine" -- is what is referred to as a Markush group.[3] Teva Br. at 20. Teva argues that "an amino acid sequence selected from the group consisting of" means that the product has one and only one of the three amino acid sequences in the Markush group. Id.

Amgen contends that Teva's use of "one and only one of the three amino acid sequences" impermissibly adds another

[3]A Markush group is a form of drafting a claim term that is approved by the PTO to serve a particular purpose when used in a claim to limit the claim to a list of specified alternatives. Gillete Co. v. Energizer Holdings, Inc., 405 F.3d 1367, 1372 (Fed. Cir. 2005). However, the term "Markush group" does not have any meaning within the context of a written description of a patent and should not be relied upon to limit its construction to the Markush group members listed in the written description. Abbott Labs. v. Andrx Pharm., Inc., 473 F.3d 1196, 1210 (Fed. Cir. 2007).

element to the claim -- an element Amgen claims is not present in the patent. Amgen Resp. at 14. Amgen argues that the term "having" signals that the structure or attributes specified thereafter are required to come within the boundary of the claim and leaving open the possibility of additional structures or attributes beyond those recited in the claim. Id. at 15. Amgen contends that this means that the claim requires that at least one of the specified amino acid sequences be present to fall within the boundaries of the claim, but this does not exclude the presence of more than one of the recited amino acid sequences. Id. at 17.

Amgen continues that "selected from the group consisting of" is a term of art that closes the set of alternative sequences to those listed as members of the Markush group, which means that only sequences from that group can meet the claim limitation. Sequences that are not listed would not satisfy this limitation of the claim. Amgen claims that nothing in the claim language excludes the presence of two or more of the amino acid sequences recited in the claim. Id.

The presence of elements in addition to those expressly recited in a patent claim cannot preclude infringement unless the claim, when properly construed, excludes the presence of such added elements. Northern Telecom Ltd. v. Samsung Elecs. Co., 215

F.3d 1281, 1296-97 (Fed. Cir. 2000)("if a patent requires A, and the accused device or process uses A and B, infringement will be avoided only if the patent's definition of A excludes the possibility of B"). Amgen argues that nothing in the claim language excludes the presence of two or more of the amino acid sequences recited in the claim, and the only sequence it does preclude is the 177-amino acid sequence of human G-CSF. Amgen Resp. at 17.

In Abbott Labs. v. Baxter Pharmaceutical Products, Inc., 334 F.3d 1274, 1281 (Fed. Cir. 2003), the Federal Circuit found that "a" (or "an," in this case) with "consisting of" meant that the patent was limited to only one member of a Markush group, i.e., the "effective amount" claimed in the patent had to be achieved by a single member of the Markush group, not by a combination of Markush group members. It did not mean that only one member of the Markush group could be present, but meant that two members of the Markush group mixed together to create an "effective amount" was not what the patentee had patented. In Abbott, the patentee could not show infringement because the defendant had not created a product that had an "effective amount" of any one member of the Markush group. Here, Teva is trying to show the opposite. Teva argues that Amgen's patents claim that there can be only one member of the Markush group

present in the product, and, if there are more, then the product is outside the scope of the patent. This construction is incorrect. Although Amgen's patents must have an effective amount of one of the versions of the patented polypeptide present in the product, it does not mean that only one of the patented versions may be present.

Teva also contends that although the "consisting of" language of the polypeptide limitation restricts the claim to one and only one of the three amino acid sequences listed in the claims, it does not exclude impurities ordinarily associated with the hpG-CSF polypeptide. Teva Br. at 21. Teva argues that all of the claim limitations should be construed to include "impurities normally associated" with the subject matter of the limitation. Teva proposes that its construction is supported by the intrinsic record because the specification of the patents-in-suit describes hpG-CSF as embracing impurities in Example 7 of the '755 patent ("[t]he final concentration of hpG-CSF was 1.5 mg/ml [and] is greater than 95% pure as determined by analysis on a gel..."). '755 patent at 16:58-60. Teva asserts that because the method of isolating the protein (hpG-CSF) is not relevant to the patent claims, Amgen's descriptions of Dr. Souza's work to clone the gene encoding the human G-CSF polypeptide and determine the amino acid sequence of that polypeptide is irrelevant to the

construction of the claims of the patents-in-suit. The claims do not require that the human G-CSF polypeptide be obtained or expressed from a cloned gene.

Teva argues that during prosecution, in order to distinguish the biochemically purified hpG-CSF in question, Amgen only needed to argue that its claimed hpG-CSF contained substantially less than 20% hpG-CSF-177, not 1% hpG-CSF. Teva Resp. at 20. But because Amgen did not do this, it failed to disclaim G-CSF polypeptide preparations containing small amounts of the 177-amino acid species. Thus, the claims must include impurities and therefore the claims will be found invalid. Teva stresses that the claims are invalid because the prior art contains only a small amount (1%), if any, of the 177-amino acid G-CSF polypeptide species, a ratio that constitutes no more than an impurity and is only a tiny fraction of the 20% of the biochemically purified hpG-CSF prior art "mixture" about which Amgen told the PTO during prosecution. Id. at 19-20.

Amgen responds that it is irrelevant whether or not the claims include impurities because the intrinsic record demonstrates that the claimed species of human polypeptide is separated from the 177-amino acid species of human G-CSF. Amgen Resp. at 20. Amgen asserts there is no doubt that the 177-amino

acid species was excluded from the claims based on the intrinsic record. Id.

We agree. During the prosecution of both patents-in-suit, Amgen argued that the claimed hpG-CSF was patentable over the biochemically purified hpG-CSF prior art on the grounds that the prior art consisted of a mixture of two types or "species" of polypeptides -- an hpG-CSF polypeptide consisting of a 174-amino acid sequence ("hpG-CSF-174") and an hpG-CSF polypeptide consisting of a 177-amino acid sequence ("hpG-CSF-177") -- whereas Amgen's claimed hpG-CSF consisted of only hpG-CSF-174. Amgen Claim Constr. Br., Ex. 18 at AMT 00002465 ('755 Prosecution History, 12/4/95 Notice of Allowability, Paper No. 31).

Amgen also stated during prosecution that the claims are directed to a 174-amino acid species of human polypeptides, and do not cover products that are not "entirely free" of the 177-amino acid species. The Examiner made clear that allowance (of the patent) was based on the fact that "the prior art always disclosed mixtures of two forms of hpG-CSF (174 and 177 amino acids in length, respectively), whereas [Amgen] has accomplished the separation of the two forms via recombinant expression, and the claims are directed to such." Id. Amgen also argues that during the prosecution of the patents the "Applicants G-CSF polypeptide as disclosed in Figure 2 is a homogenous composition

containing only 174 amino acid residues and is entirely free of the less active G-CSF 177 amino acid species." Amgen Claim Constr. Br., Ex. 17 at AMT 00002430 ('755 Prosecution History, 12/4/95 Notice of Allowability, Paper No. 31).

Teva argues that under Conoco Inc. v. Energy & Envl. Int'l, L.C., 460 F.3d 1349, 1360 (Fed. Cir. 2006), all claim limitations are construed to include "impurities normally associated" with the subject matter of the limitations. Teva Br. at 21; Teva Resp. at 14. Conoco is distinguishable because, unlike that case -- where the Federal Circuit held that impurities commonly associated with the claimed invention are not excluded from the scope of the claim even if the claim includes language that would normally close a claim element to unrecited elements -- here there is no doubt that the 177-amino acid species was excluded from the claims based on the intrinsic record. Based on the prosecution history, Amgen's construction is correct. The entire basis of the patent is Dr. Souza's invention of a 174-amino acid species that is "entirely free" of the 177-amino acid species. We will adopt Amgen's construction.

C. "Isolated" (Claim 1 of the '755 patent)

Claim Term	Amgen's Construction	Teva's Construction
"isolated"	separate from forms of human G-CSF not having the amino	separated from other substances

	acid sequences recited in the claim	

Teva argues that "isolated" means "separated from other substances." Teva Br. at 23. The specification acknowledges that "isolated" hpG-CSF was known: "[a]nother factor, designated human CSF-β, has also been isolated from human bladder carcinoma cell line 5637." Id. at 23;'755 patent, 6:5-9. Teva asserts that although "isolated" means "separated from other substances," this does not mean "free of impurities." Teva Br. at 24. Teva also argues that Amgen could have defined "isolated" however it wanted to but declined, and that when it filed new claims with the term "isolated" and removed "non-naturally occurring," Amgen made clear that the two phrases have different meanings. Id. at 25-26.

Amgen submits that the term "isolated" means "set apart" or "standing alone." Amgen claims that in the context of claim 1 of the '755 patent "isolated" modifies "hpG-CSF polypeptide," and therefore it reinforces that the claimed polypeptides are separated from hpG-CSF polypeptides not having the amino acid sequences recited in the claim, i.e., the claims do not encompass the 177 form. Amgen Br. at 30. Amgen points out that both parties agree that the plain meaning of the term "isolated" is "separated" or "set apart." The parties agree that

"isolated" and "pure" are different concepts, and that "isolated" does not preclude the presence of at least some other substances in addition to the claimed polypeptides.

The parties disagree, however, on whether "isolated" is properly construed apart from the claim phrase it modifies. Amgen claims that Teva fails to specify exactly what it is that is separated and ignores a defining characteristic of Dr. Souza's claimed invention, namely, the isolation of a particular species of hpG-CSF polypeptide. Amgen Resp. at 11. Amgen proposes that "an isolated human pluripotent granulocyte colony stimulating factor (hpG-CSF) polypeptide" means a separated species of human polypeptide, designated hpG-CSF. That separate species is necessarily separate from hpG-CSF polypeptides not having one of the specified amino acid sequences, and therefore excludes the 177-amino acid species of hpG-CSF. Id.

Amgen claims that the intrinsic record supports its view because, before Dr. Souza's invention, the art lacked an ability to produce or obtain the claimed species of hpG-CSF polypeptides in isolation. Dr. Souza provided a means to produce and obtain that species of hpG-CSF polypeptides separate and apart (i.e., isolated) from all of the other polypeptides and substances produced in the human cancer cells that had thwarted prior attempts to achieve that result. Id. at 12. Amgen asserts

that, properly construed, the term "isolated" serves to reinforce the fact that the species of hpG-CSF polypeptide claimed by Dr. Souza is separate from other species of hpG-CSF polypeptides whose amino acid sequences differ from those recited in Dr. Souza's claims. Id. at 13.

Amgen argues that Teva's construction would render the second claim in the '755 patent[4] -- which is dependent upon the first claim -- meaningless because it is a composition claim that must contain the isolated polypeptide of claim 1 and a carrier, and expressly allows for the presence of additional substances. Teva's construction, "separated from other substances," would render claim 2 meaningless because it would require the polypeptide to be both separated from other substances and combined with other substances. The Federal Circuit has deemed this sort of construction impermissible. Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc., 520 F.3d 1358, 1362 (Fed. Cir. 2008)("this court strives to reach a claim construction that does not render claim language in dependent claims meaningless"). Thus, we agree with Amgen and will adopt its construction.

D. "A Method for Providing Granulocytopoietic Therapy to a Mammal" ("Granulocytopoietic Therapy") (Claim 2 of the '823 patent)

[4]The second claim of the '755 patent is "[a] composition comprising the hpG-CSF polypeptide of claim 1 and a carrier."

Claim Term	Amgen's Construction	Teva's Construction
"granulocytopoietic therapy"	therapeutically treating a mammal by stimulating the production of granulocytes	treatment that causes an increase in the number of, or development of, granulocytes

Claim 2 of the '823 patent is directed to "a method for providing granulocytopoietic therapy to a mammal." Teva proposes that we construe "granulocytopoietic therapy" as "treatment that causes an increase in the number of, or development of, granulocytes." Teva Br. at 26. Amgen proposes that the limitation means "a method for therapeutically treating a mammal by stimulating the production of granulocytes." Amgen Br. at 30. Teva notes that this leaves the definition of "therapy" undefined. Teva Br. at 27.

Teva argues that we should reject Amgen's proposed construction because it does not provide a complete definition of the limitation. Id. Teva claims that a person of ordinary skill in the art would understand that the term "granulocytopoietic" refers to the production/proliferation of granulocytes. Id. Teva claims that the term therapy has its plain and ordinary meaning, i.e., treatment. Id. at 28. Thus, Teva argues, "granulocytopoietic therapy" should be construed as the treatment

that causes an increase in the number, or development of, granulocytes. Id. at 29.

Amgen agrees that "granulocytopoietic" means "the development of granulocytes." Amgen Br. at 31. But the parties differ on the definition of "therapy." Amgen argues that Teva's proposed construction improperly equates "therapy" with "treatment" and argues that Teva's construction would expand the claim scope to cover any increase in the number or development of granulocytes, regardless of whether the method achieves a therapeutic or remedial benefit to a mammal, as required by the claim language. Amgen Resp. at 23. Amgen contends that Teva's definition could theoretically involve nothing more than a medically inconsequential increase in the number of granulocytes, or a harmful and detrimental overproduction of granulocytes, neither of which constitute "therapy" as the claims require. Id. Amgen argues that "treatment" does not go far enough. It is "treatment" to alleviate or cure a condition. Medical dictionaries define "therapy" as the "treatment of disease." Id. Amgen claims that its construction embodies the therapeutic requirement of the claim but Teva's construction does not. Id.

Amgen also argues that Teva's construction reads the term "mammal" out of the claim, changing the meaning of the phrase from therapeutically treating a mammal to a definition

that encompasses treating cells in a petri dish. Id. at 24. Finally, Amgen disputes the relevance of Teva's contention that the specification does not disclose examples of providing treatment to mammals, thus implying that the claim cannot be directed to providing therapy to a mammal. Id. at 25.

The term "granulocytopoietic therapy" does not appear in the specification (except in the claim itself). But in fair summary, the preamble states that the method must provide therapy to a mammal granulocytopoietically (i.e., by stimulating the production of granulocytes). In general, a claim preamble is limiting if it recites essential structure or steps, or if it is "necessary to give life, meaning, and vitality" to the claim. Intirtool, Ltd. v. Texar Corp., 369 F.3d 1289, 1295 (Fed. Cir. 2004). Here, the preamble is "necessary to give life, meaning, and vitality" to the claim and it must be construed as a claim limitation. Catalina Marketing Int'l, Inc. v. Coolsavings.com, Inc., 289 F.3d 801, 808 (Fed. Cir. 2002). Thus, the word "mammal" cannot be read out of the claim, and the term must encompass the limitation of providing therapy to a mammal.

In addition, although the examples in the specification do not disclose examples of providing therapy to a mammal, a claimed invention is not limited to the examples provided in the specification, but rather is defined by the words in the claims.

Specialty Composites v. Cabot Corp., 845 F.2d 981, 987 (Fed. Cir. 1988)(finding that the patent is not restricted to the examples, but rather is defined by the words in the claim); Dow Chemical Co. v. United States, 226 F.3d 1334, 1342 (Fed. Cir. 2000)(noting that, as a general rule, claims of a patent are not limited to the examples listed within the patent specification).

Amgen does ultimately define "therapy" in its response as "a medical or therapeutic benefit." Amgen Resp. at 23. Amgen stated that the present invention "has been proven to be clinically effective, and is the first therapeutic product which can be used to effectively treat the hundreds of thousands of chemotherapy patients who suffer from a dangerous drop in white blood cell counts, and to treat other disorders involving low white blood cell counts." Amgen's Br., Ex. 13 at AMT 00002363 ('755 Prosecution History, 5/29/90 Amendment D, Paper No. 9). We will adopt Amgen's construction because "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." Renishaw PLC v. Marposs Societa' per Azioni, 158 F.3d 1243, 1250 (Fed. Cir. 1998). Amgen's product is meant to treat mammals therapeutically, and its construction encompasses that aim.

E. "Administering an Effective Amount of" (Claim 2 of the '823 patent)

Claim Term	Amgen's Construction	Teva's Construction
"administering an effective amount of"	administering an amount adequate and suitable for therapeutic use	to give an amount sufficient to cause a desired effect

Teva proposes that "administering" be given its plain and ordinary meaning: "to give." Teva Br. at 29. Teva argues that this construction is supported by the intrinsic record of the specification and the prosecution history because "administering" is used to describe "giving" hpG-CSF to cell cultures and mammals. Id. Amgen responds that this definition is too broad, that "administering" actually implies a remedial use for a mammal and not just "to give," and that "administering," read together with the preamble in the context of therapeutically treating a mammal, does not simply mean giving to cells in a petri dish. Amgen Resp. at 26-27. We find that Amgen's construction is correct because "administration," as used in the context of providing therapy, requires more than merely "giving" a dose of a substances to a cell culture. Decl. of J. Wolfson in Support of Teva's Opening Brief on Claim Construction, Ex. 23 (Webster's 1986).

With regard to "an effective amount," Teva argues that "effective" generally means "capable of bringing about an

effect." Teva Br. at 31. Teva argues "effective amount" should mean an amount of hpG-CSF sufficient to cause a desired effect of hpG-CSF increasing the number of granulocytes. Id. Teva contends that a person of ordinary skill in the art would understand that an "effective amount" is an amount of hpG-CSF that can elicit the desired effects named in the specification. Id. at 31-32.

Amgen argues that reading the "effective amount" limitation in conjunction with the preamble indicates that the term refers to the amount effective to treat a mammal therapeutically by stimulating the production of granulocytes. Id. That is, the '823 patent claim 2 requires that hpG-CSF be present in a quantity and quality sufficient to prevent, cure, or alleviate life-threatening and debilitating conditions in a mammal by stimulating the production of granulocytes. Id. Amgen argues that an "effective amount" is an amount that is both adequate and suitable for therapeutic use. Amgen Br. at 33. Amgen claims that this construction is supported by the specification, which states that pharmaceutical compositions "useful in hpG-CSF therapy" must comprise "effective amounts" of hpG-CSF. Id. at 34; '755 Patent at 4:24-27.

Amgen contends that Teva's construction should be rejected because it does not reference the required therapeutic

objective and further ignores the full implication of "effective," which requires an hpG-CSF product that is both suitable and adequate for therapeutic use. Amgen Resp. at 27. According to Amgen, Teva's construction does not use "effective amount" in terms of an amount effective for therapy -- administering a minuscule amount to cause inconsequential increases in the number of granulocytes, as well as administering an overdose of hpG-CSF to cause death, would both fall within the scope of the claims as Teva defines them. Id.

"Effective amount" has a customary usage. Abbott Labs. v. Baxter Pharm. Prods., Inc., 334 F.3d 1274, 1277 (Fed. Cir. 2003). Here, the term would mean the amount of a hpG-CSF polypeptide that will provide "granulocytopoietic therapy to a mammal." '823 Patent, Claim 2.

We must take the preamble into account in determining the proper construction for the meaning of "an effective amount." Again, a claim preamble is limiting if it recites essential structure or steps, or if it is necessary to give life, meaning, and vitality to the claim. Intirtool, 369 F.3d at 1295.[5] An "effective amount" should be an effective amount for "providing

[5]A preamble may also provide context for claim construction, particularly where that preamble's statement of intended use forms the basis for distinguishing the prior art in the patent's prosecution history. Metabolite Labs., Inc. v. Lab. Corp. Of America Holdings, 370 F.3d 1354, 1362 (Fed. Cir. 2004).

granulocytopoietic therapy to a mammal," as the full claim states. "Effective amount" must be an amount effective for therapy.

Teva cites Amgen Inc. v. Hoechst Marion Roussel, Inc., 457 F.3d 1293 (Fed. Cir. 2006), to support its position that "effective amount" should mean "to give an amount sufficient to cause a desired effect," claiming that "a desired effect" is an amount that will cause any one or all of the effects listed in the specification. Teva Br. at 31. But, in Amgen v. Hoechst Marion Roussel, the claim in question specified only "[a] pharmaceutical composition comprising a therapeutically effective amount of human erythropoietin and a pharmaceutically acceptable diluent, adjuvant or carrier, wherein said erythropoietin is purified from mammalian cells grown in culture." Id. at 1300. In that case, Amgen argued that a "therapeutically effective amount" meant that there would be an increase in hematocrit as well as any or all of the biological effects previously attributed to the natural version of the patented product. Id. at 1301. This case is different. Amgen argues only that "effective amount" must be an amount effective to provide therapy to a mammal. That language is written into the claim itself and must be given effect. We therefore agree with Amgen that Teva's construction must be rejected because it does not reference the

required therapeutic objective. Amgen Resp. at 27. We will adopt Amgen's construction.

V. Conclusion

We will construe the first term, "pluripotent," according to Teva's proposed construction, but the rest of the terms we will construe according to Amgen's proposed constructions.

BY THE COURT:

__\s\Stewart Dalzell